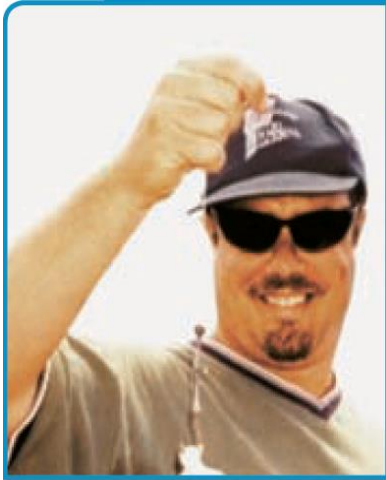




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Inflammatory Arthritis A to Z - Concurrent Workshop

Saturday, 17 August 2013

Start 4:30pm

Duration: 60mins Collosseum



South GP CME 2013

General Practice Conference & Medical Exhibition

15-18 August | Edgar Centre | Dunedin

Investigating, treating and referring suspected inflammatory arthritis.

Introduction

- Perhaps the most critical issue in the initial assessment of a patient presenting with symptoms of arthritis is to determine whether or not the symptoms result from inflammation or not.
- This is because inflammatory problems usually ultimately stem from immune system activity, and require immunosuppressive treatment.
- This approach that is both ineffective, and potentially harmful, in non-inflammatory conditions.

Distinguishing Inflammatory from non-inflammatory disease

- Usually, the distinction between inflammatory and non-inflammatory disease is easy.
- However, the distinction between inflammatory and non-inflammatory conditions can be one of the most difficult challenges in assessing patients with joint or musculoskeletal pain.
- The difficulty arises because occasional patients with inflammatory disease have normal inflammatory markers on blood testing and little or no evidence of inflammation on physical examination.
- **Neither the degree of pain present, nor the degree and duration of morning stiffness have any utility in distinguishing inflammatory from non inflammatory disease.**
- **Patients with inflammatory sounding histories (ie pain with prominent morning and inactivity stiffness, or swelling) must have an ESR and CRP done and a physical examination.**
- ESR and CRP usually correlate, but it is not uncommon for one to be markedly elevated whilst the other is normal or marginally raised.

Inflammatory vs Non-Inflammatory disease

- In the primary care setting, more patients presenting with pain and stiffness are going to have fibromyalgia than inflammatory arthritis.
- Fibromyalgia should be considered when a patient presents with what sounds a convincing history of inflammatory arthritis, but both the physical examination and laboratory data provide no objective evidence of inflammation.
- Fibromyalgia needs to be included in the differential diagnosis early (at the first visit), rather than after several rounds of visits and negative investigations.
- If fibromyalgia is being considered, evidence that supports a diagnosis of fibromyalgia should be sought.

Fibromyalgia

- Features supportive of fibromyalgia include:
 - **Abnormal pain response.** Usually this can be abundantly demonstrated by applying reasonably firm pressure to one or two trigger points. It is not necessary to test 18 trigger points, as the diagnosis is usually well and truly made after pressing 2 or 3 trigger points.
 - Usually testing for tenderness at the lateral epicondyle of the elbows, trochanteric regions, upper posterior buttock and anterior chest is sufficient.
 - Fibromyalgic patients have (objectively measured in experiments) increased pain responses to relatively benign stimuli.
 - **Poor and/or unrefreshing sleep.**
 - **Chronic fatigue.**
 - **Widespread paraesthesiae.**
 - **Cognitive impairment – “fibro fog.”**
 - **Irritable bowel or bladder symptoms.**
 - **Migraine or headaches.**

Diagnostic considerations in Inflammatory Arthritis

- Septic arthritis

- Patients presenting with a single hot swollen joint may have septic arthritis (gout being the major differential) and should be referred to the Orthopaedic or Emergency Departments for initial workup and management.

- Vasculitis/SLE

- Patients with multi-organ disease (eg with prominent skin rash – especially petechial shin rash), respiratory (upper or lower respiratory tract) involvement, mononeuritis multiplex, or active urinary sediment), or in whom there is a strong clinical suspicion of vasculitis should be discussed urgently with the rheumatologist or physician on call.

Inflammatory arthritis

- Once objective evidence of inflammation is found (elevated inflammatory markers and/or objectively inflamed joints), attention should turn to diagnosis and initial management.
- Patients with less than 6 weeks of symptom duration can reasonably be treated with a short course of prednisone (eg 20mg/15mg/10mg/5mg daily each for a week then stop), assuming simple NSAIDs (where not contraindicated) and paracetamol have not sufficiently controlled symptoms.
 - This enables “weeding out” of the group of patients in whom disease is a monophasic illness only.
- Patients who develop recurrent inflammation or who present with more than 6 weeks of inflammation should have diagnostic tests performed (ESR, CRP, Rheumatoid factor, anti-CCP antibodies, ANA, ENA, dsDNA, urinalysis, FBC, U+E, LFT).
- HLA B27, Urate, Hepatitis B and/or C serology and cryoglobulins may be appropriate in selected cases).

DMARD therapy

- A decision to institute long term DMARD therapy should only be undertaken when there has been persistent or recurrent inflammation, or if a definite diagnosis of rheumatoid arthritis has been made.

Diagnosis of Inflammatory Arthritis

- **Major diagnostic considerations** at this point include (but are not limited to):
 - Rheumatoid Arthritis
 - Psoriatic Arthritis
 - Lupus/Connective tissue disease/ANA associated arthritis
 - Spondyloarthropathy (includes ankylosing spondylitis, reactive arthritis, IBD-associated arthritis, Psoriatic spondyloarthropathy)
 - Polymyalgia Rheumatica
 - Gout

Rheumatoid Arthritis

- Rheumatoid classically presents as a symmetrical inflammatory polyarthritis with a predilection for the wrists, MCPs, PIPs, and MTPs. The larger joints are often also involved.
- Several studies since the late 1990s have informed what has become a key principle of RA treatment:
 - A strategy of aggressive, early treatment of rheumatoid arthritis results in joints deteriorating (as measured by serial X-rays) at a significantly lesser rate compared to a less intensive early treatment regimen.
 - As radiographic deterioration is the single most important determinant of disability in the long term, an early, aggressive response to RA, with multiple DMARDs if necessary, has become the standard approach.
 - Thus **early, accurate identification of Rheumatoid Arthritis is very important.**

Rheumatoid Arthritis -diagnosis

In 2010 the American College of Rheumatology and the European League Against Rheumatism collaborated in the creation of modern classification criteria for the identification of RA.

2010 ACR/EULAR Classification Criteria for RA	
JOINT DISTRIBUTION (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
SEROLOGY (0-3)	
Negative RF <u>AND</u> negative anti-CCP antibodies	0
Low positive RF <u>OR</u> low positive anti-CCP antibodies	2
High positive RF <u>OR</u> high positive anti-CCP antibodies	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
≥6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP <u>AND</u> normal ESR	0
Abnormal CRP <u>OR</u> abnormal ESR	1

≥6 = definite RA

What if the score is <6?

Patient might fulfill the criteria...

→ **Prospectively** over time
(cumulatively)

→ **Retrospectively** if data on all
four domains have been
adequately recorded in the past

Clinical context is important
as false positive classification
is possible.

- For example a patient with inflammatory osteoarthritis might have an objectively inflamed PIP joint and score 6 as follows:
 - One clinically inflamed OA joint (PIP 3 right hand) = **eligible**
 - Tenderness of all DIPs, PIPs, thumb IPs, CMC 1, and knees = **score 5 points** for 10 joints (PIPs, thumb IPs, knees)
 - Seronegative = **score 0 points**
 - Symptom duration 6 weeks = **score 1 point**
 - Negative acute phase reactants = **score 0 points**

Psoriatic Arthritis

- Approximately 30% of patients with psoriasis have an associated arthropathy.
- There is scant relationship between the skin and joint disease – one can be extremely active whilst the other is quiescent and *vice-versa*.
- The cutaneous aspects of psoriasis can be very subtle. Careful search including skin (elbows, knees, natal cleft, beneath breasts), scalp (posterior neck line and behind ears) and nails (onycholysis or pitting) is mandatory in an undiagnosed inflammatory arthropathy.
- However a personal history of psoriasis is not absolutely necessary to make the diagnosis: a family history of a first degree relative with psoriatic arthritis confers enough of a genetic legacy to make patients susceptible to the arthritis.

Psoriatic Arthritis

- Classically there are 5 recognised patterns of psoriatic arthritis:
 - Asymmetrical oligoarticular arthritis
 - Symmetrical polyarthritis
 - Distal interphalangeal arthropathy
 - Arthritis mutilans
 - Spondylitis with or without sacroiliitis
- Identification of the particular subtype is not especially important clinically; it is important to recognise that psoriatic arthritis can present in myriad ways.
- Dactylitis (sausage digit, swelling of the entire digit) is a characteristic feature of psoriatic arthritis (can also occur in HLA B27-associated spondyloarthropathies). When present in a psoriatic patient it is virtually pathognomic of psoriatic arthritis.
- DIP joint involvement is only present in psoriatic arthritis and osteoarthritis. This important distribution characteristic can be very helpful diagnostically.

ANA-related arthritis /Connective Tissue Disease / SLE

- **What does this positive ANA mean?" is a common question.**
 - Antinuclear antibodies when measured in unselected populations are usually false-positives.
- In the absence of the clinical features below, ANA is not likely to be relevant.
- The clinical features common to both mild (much more common) and more severe ANA-related disease are:
 - Photosensitivity
 - Lethargy (often profound)
 - Small joint polyarthralgia / polyarthritis with morning and activity stiffness. The arthralgia is often severe with no obvious clinical signs such as redness or swelling. It often is somewhat migratory appearing in different areas on different days or even within hours.
 - Dryness of the eyes and/or mouth
 - Raynaud's Phenomenon
- Less common, and more typical of full-blown lupus are:
 - Alopecia
 - Mouth Ulcers (severe)
 - Malar rash
 - Serositis (pleurisy/pericarditis/abdominal serositis)

Autoantibody titre / pattern / associations.

- ANA is rarely relevant if it is present in a titre of less than 1:320. Lesser titres such as 1:80 can be relevant if there are several clinical features from the above list present, but this is uncommon; typically patients with some or all of the above features will have titres of 1:1280 or greater.
- ANA pattern. Most patterns (speckled, homogenous, peripheral) are not particularly useful in routine clinical day-to-day practice. Associated ENAs (extractable nuclear antigens) are more useful when they are present.
- **An exception is the anticentromere pattern. This is associated with the CREST variant of limited scleroderma and when encountered should prompt specific enquiry for the features of CREST syndrome:**

Medscape®		www.medscape.com	
Peripheral (rim)		anti-DNA (not seen on HEp-2)	SLE
Homogeneous (diffuse)		anti-DNA anti-histone anti-DNP (nucleosomes)	RA & SLE Misc. Disorders (anti-ssDNA)
Speckled		anti-Sm & RNP anti-Ro & La anti-Jo-1 & Mi-2 anti-Scl-70	SLE & SS PM/DM PSS (Systemic)
Centromere		anti-centromere	PSS (CREST)
Nucleolar		anti-nucleolar	SLE & PSS

CREST syndrome:

- **Sclerodactyly.** (a fat, “sausagey” appearance of the fingers is typical in CREST, rather than the classical tight, tethered, fibrosed appearance of diffuse scleroderma)



- **Raynaud's phenomenon.** Can be severe. Multiple periungual infections and pitting scars on the tips of the fingers are clinical markers of Raynauds' severity.
- **Esophageal symptoms.** Both reflux and dysmotility should be enquired about. Occasionally the whole gut can be affected.
- **Calcinosis.** Reasonably uncommon. Can occur anywhere, but commonest to have small lesions in the finger pulps (distal phalanges).
- **Telangiectasiae.** Face and fingers/palms. Rarely clinically important.

ANA/ENA associations:

- Extractable nuclear antigens (ENAs) when present make it much less likely that ANA is false positive.
- Sjogren's syndrome is where ENAs are most often clinically useful. A typical Sjogren's patient will have strongly positive ANA, positive Ro (also known as SSA) and/or La (also known as SSB) antibodies, very often a positive rheumatoid factor, elevated ESR and normal/ near normal CRP.
- Anti-dsDNA is important as it is highly specific for lupus, and either confirms the diagnosis in patients with features of connective tissue disease, or should prompt vigilance in monitoring for these features. Most features are clinically symptomatic but renal disease can be clinically silent and should be regularly screened for with MSU and U+E (approx 3 monthly) in patients who are dsDNA positive

Spondyloarthropathy (includes ankylosing spondylitis, reactive arthritis, IBD-associated arthritis and psoriatic spondyloarthropathy)

- The hallmark of the spondyloarthropathies is the predilection for inflammation to occur at the entheses
 - (entheses = point of insertion of tendon/ligament into bone).
 - The spine and sacroiliac joints have multiple ligaments/entheses and are characteristically involved, although pure peripheral joint presentations can occur. In adolescents, for example, a single inflamed ankle or knee joint is a common presentation of spondyloarthropathy and an HLA B27 should be checked.
 - Family or personal histories compatible with spondyloarthropathy, inflammatory bowel disease and psoriasis should be sought if spondyloarthropathy is suspected.
 - Preceding infections (especially diarrhoeal – much more common than urethral) should be enquired into.

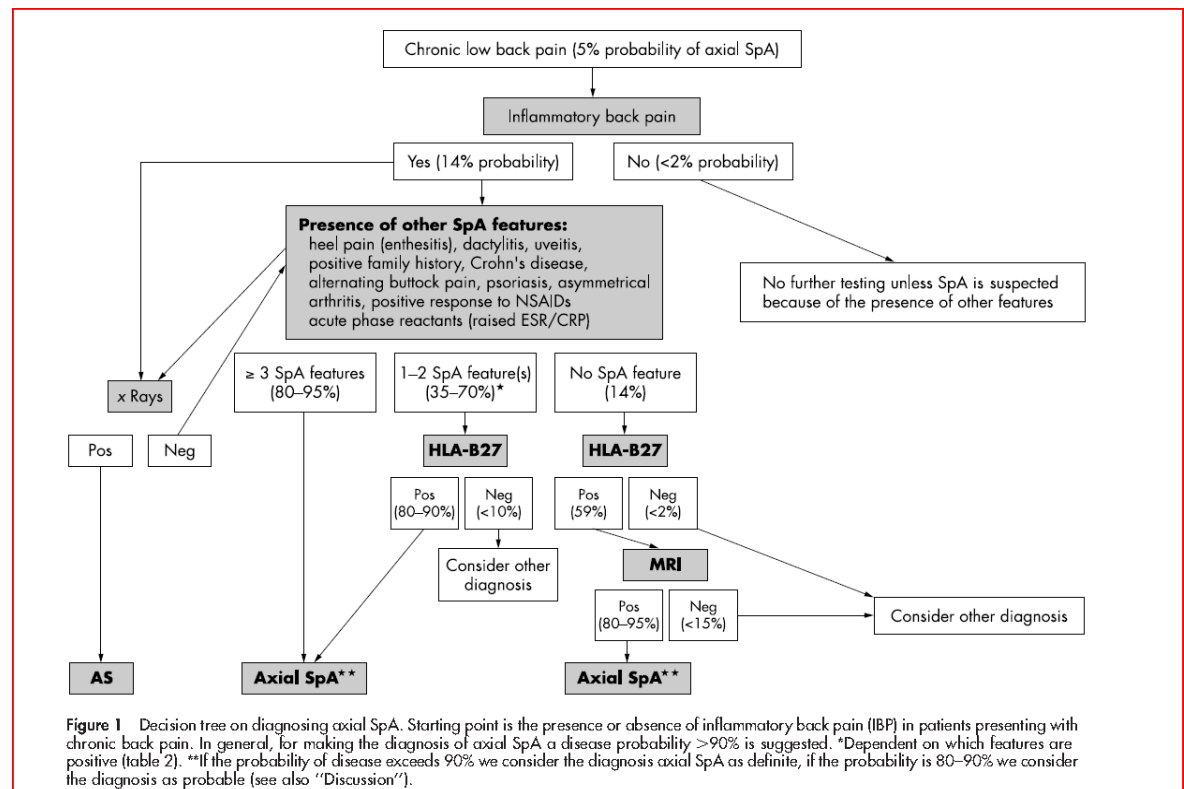
Clinical features characteristic of spondyloarthropathies:

- **HLA B27 positivity.** 95% of Ankylosing Spondylitis patients are HLA B27 positive. Approximately 3-8% of the background population are B27 positive, of whom only about 5% will develop the disease.
- **Family history.** B27 positivity **AND** a family history of Ankylosing Spondylitis confers approximately a 30% risk of Ankylosing Spondylitis.
- **Iritis/Uveitis.** A characteristic feature of the spondyloarthropathies. Usually presents with red, aching, photophobic eye(s). There may only be a reduction in vision noted. Uveitis/Iritis is important as a diagnostic clue. It is also important that patients are educated about the potential for iritis/uveitis to occur, so that they seek help early if inflammatory eye symptoms occur. Untreated it is sight-threatening.
- **Heel pain (Achilles tendinitis and plantar fasciitis).** The most common and diagnostically important extra-axial examples of enthesitis.
- **Sacroiliitis.** Presents as unilateral, bilateral or alternating buttock pain.
- **Dactylitis.** A swollen reddened digit.
- **Raised inflammatory markers.** However, spondyloarthropathy is notorious for often having very active inflammation that is not reflected in the ESR or CRP so negative inflammatory markers do not rule out the disease.
- **Positive response to NSAIDs.** Non-specific low back pain has a roughly 15-20% response rate to NSAIDs, whereas spondyloarthropathy patients typically report response rates of 75% or greater.



Diagnosing Spondyloarthropathy.

- Unselected back pain presenting to primary care has approximately a 2-5% likelihood of being due to inflammatory spondyloarthropathy.
- Even if the pattern of pain is inflammatory in its characteristics (worse with rest, improved with activity) then the likelihood of spondyloarthropathy is still only around 14-18%.
- The greater number of associated clinical features that are present, the greater the likelihood of the diagnosis. This can be represented diagrammatically.



Gout.

- Gout is usually easy to differentiate from other inflammatory arthritis.
- It is important to diagnose accurately and early as the treatment is completely different from the other inflammatory arthritides, where a very considerable degree of therapeutic overlap exists.
- The intensity of the inflammatory reaction is extreme, and the speed of onset of symptoms and the severity and degree of inflammation are extreme also.
- Onset of pain is very rapid – from normality to excruciating pain in a few hours (very often overnight). Experienced patients often speak of a tingling or itchy sensation in the joint for a few hours before the inflammation proper then sets in.
- The pain of a gouty joint is utterly exquisite, classically the weight of a bedsheet being intolerable.
- The heat, redness and swelling are often far in excess of what is seen in the other inflammatory arthritides. Classically of course, the 1st MTP is affected, and 90% of all gout patients will have 1st MTP involvement at some stage.

Gout.

- Usually the most important differential diagnosis in gout is septic arthritis, and there should be a low threshold for seeking orthopaedic input to rule out sepsis in new presentations, especially if not in first MTP.
- The intensity of the immune reaction to gouty crystals mean that fever, very high CRPs and markedly elevated WBC counts can often occur in gout, particularly in polyarticular presentations, so none of these features has great utility in distinguishing sepsis and gout.
- The serum urate is of poor utility in the presence of acute inflammation, as in acute gout. **A normal or low serum urate level is seen very often in acute gout.** Increased clearance of uric acid by the kidney in acute inflammatory states is thought to be responsible (not the uric acid all disappearing into the joints).
- Aspiration of an affected joint looking for negatively birefringent monosodium urate crystals is the diagnostic test of choice. (Sepsis is also checked for at the same time). Samples **must** be sent promptly to the laboratory. Many technical factors between the bedside and the microscope can, and very often do, lead to false negatives occurring. Joint aspirates for crystals should never sit overnight before analysis, for example.
 - Sending samples in a green-top tube preserves the crystals and false negatives are less frequent

Initial Management of Inflammatory Arthritis

- As stated earlier, a decision to institute long term DMARD therapy should only be undertaken when there has been persistent or recurrent inflammation, or if a definite diagnosis of rheumatoid arthritis has been made.
- Gout is treated completely differently to the other arthritides, and will be briefly covered at the end of this section.
- For the bulk of the inflammatory arthritides, the basic pharmacological armamentarium is the same and consists of:
 - Methotrexate
 - Leflunomide (Arava)
 - Hydroxychloroquine (Plaquenil)
 - Sulphasalazine (Salazopyrin)
 - Prednisone
 - Azathioprine

Collectively known as the DMARDs
- Cyclosporine and intramuscular gold are potentially available but are only rarely utilised. Their use is probably best restricted to Rheumatologists.
- Biological agents (anti-TNF, anti B-cell, anti-IL-6 and other agents) are also restricted to Rheumatologists.

Initial Management of Inflammatory Arthritis

- Note that methotrexate and leflunomide are completely contraindicated in pregnancy and breastfeeding.
- DMARDs used to be known as the SAARDs (slow-acting anti-rheumatic drugs), and they take approximately 3 months to exert their full therapeutic action.
- Prednisone on the other hand acts immediately, and more often than not, patients will need concomitant prednisone whilst the effect of the DMARD is awaited.

Initial Management of Inflammatory Arthritis

- Obviously pharmacological therapy needs to be individually tailored to the patient, but my personal practice is to utilise the following agents, generally in the following order:

Diagnosis	1 st DMARD	2 nd DMARD	3 rd DMARD	4 th DMARD
Rheumatoid Arthritis	Methotrexate	Hydroxychloroquine	Sulphasalazine	Leflunomide
Psoriatic Arthritis	Methotrexate	Leflunomide	Sulphasalazine	Hydroxychloroquine
Lupus/ connective tissue disease	Hydroxychloroquine	Prednisone	Azathioprine	
Spondylo-arthropathy	NSAID/physiotherapy	Sulphasalazine for peripheral joint involvement	TNF inhibitors	

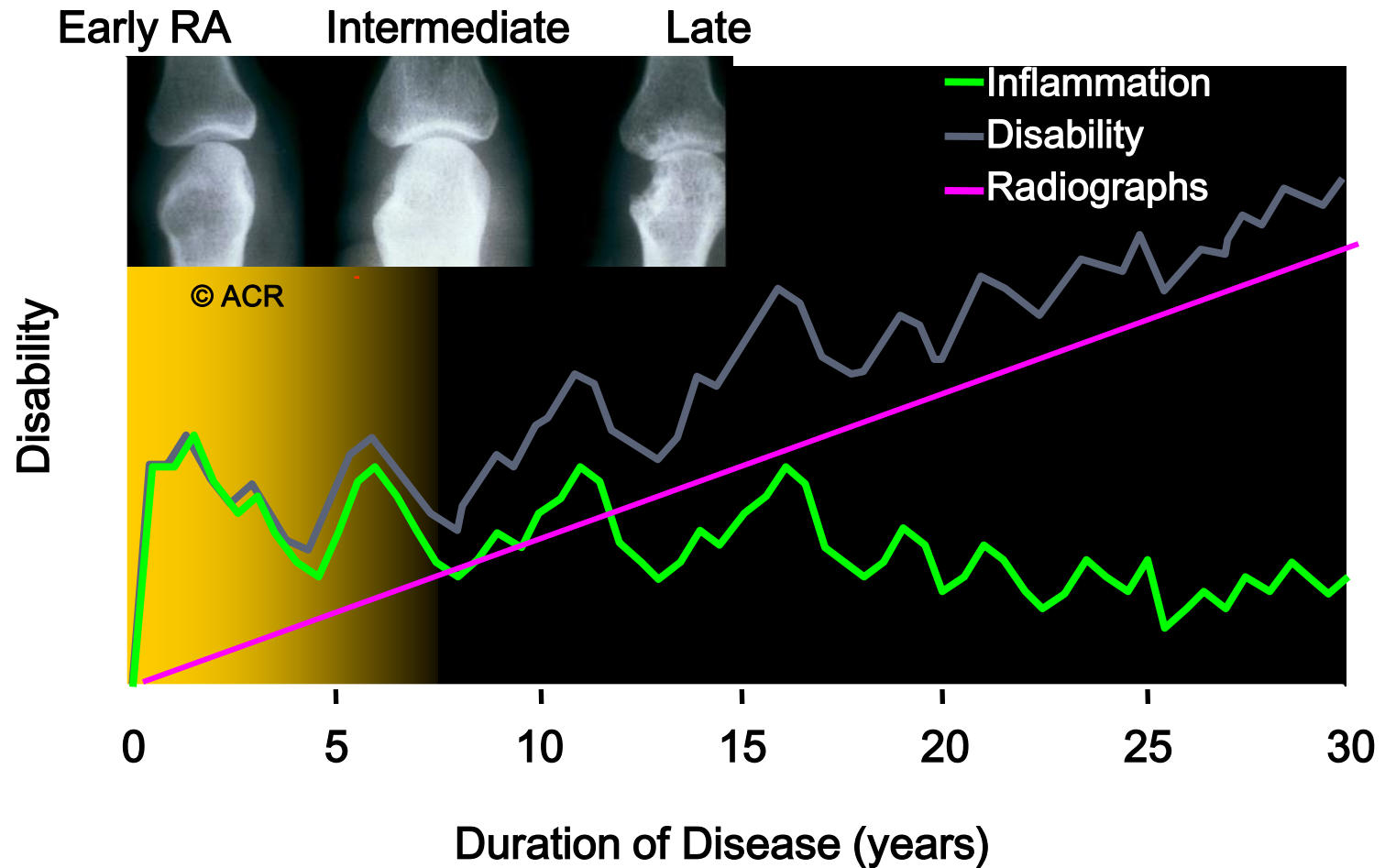
Initial Management – Rheumatoid Arthritis

- Methotrexate has firmly established itself worldwide as the preferred anchor treatment around which RA treatment is based.
- Several trials have demonstrated that an initial aggressive approach (either with multiple DMARDs +/- prednisone, or with methotrexate plus an anti-tumour necrosis factor agent) is superior to an initial single DMARD strategy with sequential stepping up of therapy.
 - Higher rates of remission, faster return of function and slower rates of radiographic deterioration have all been repeatedly shown across multiple studies.
- However it is also well recognised that many patients do respond very well to methotrexate monotherapy alone.

Initial Management – Rheumatoid Arthritis

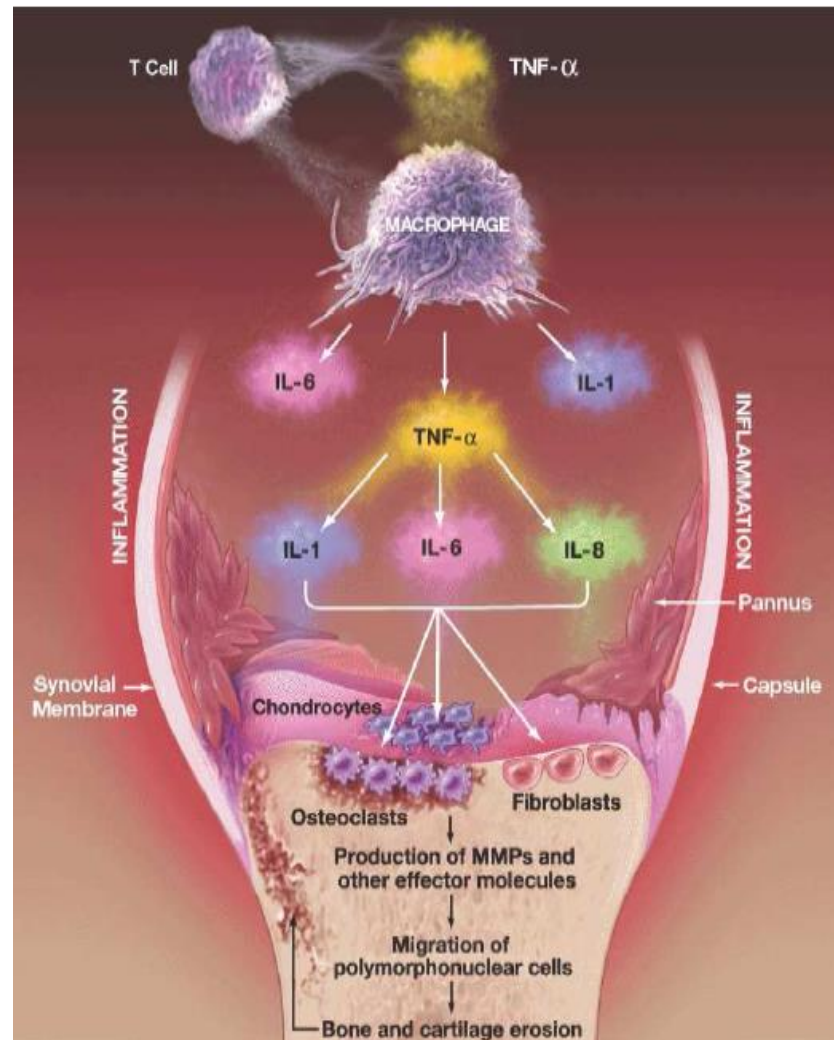
- One of the challenges of RA treatment is **to achieve rapid and complete remission of disease** (as defined by constructs such as the DAS – disease activity score – (which is a standardised composite measure calculated from inputs including the number of tender and/or swollen joints, ESR or CRP, and a patient self-assessment), **whilst avoiding excessive medication**.
- This is achieved in many centres by commencing the patient on methotrexate and observing the response after 3-4 months of therapy. Up to 35% of patients enter complete remission with methotrexate alone. Methotrexate is then continued indefinitely.
- Non-responders have rapid and aggressive escalation of therapy according to local practice.
- **In Europe and the USA this often means moving immediately to anti-TNF inhibitor therapy in combination with methotrexate.**

Why anti-TNF drugs?



Adapted from Kirwan JR. *J Rheumatol.* 2001;28:881-886.

Why anti-TNF drugs?



(Modified) Sharp score



Erosion: 8-point scale with
0.5 increments
14 sites/hand

0= normal
0+= questionable
1= mild (1.45 mm)
1+= mild, worse
2= moderate (2mm)
2+= moderate, worse
3= severe (2.83 mm)
3+= severe, worse

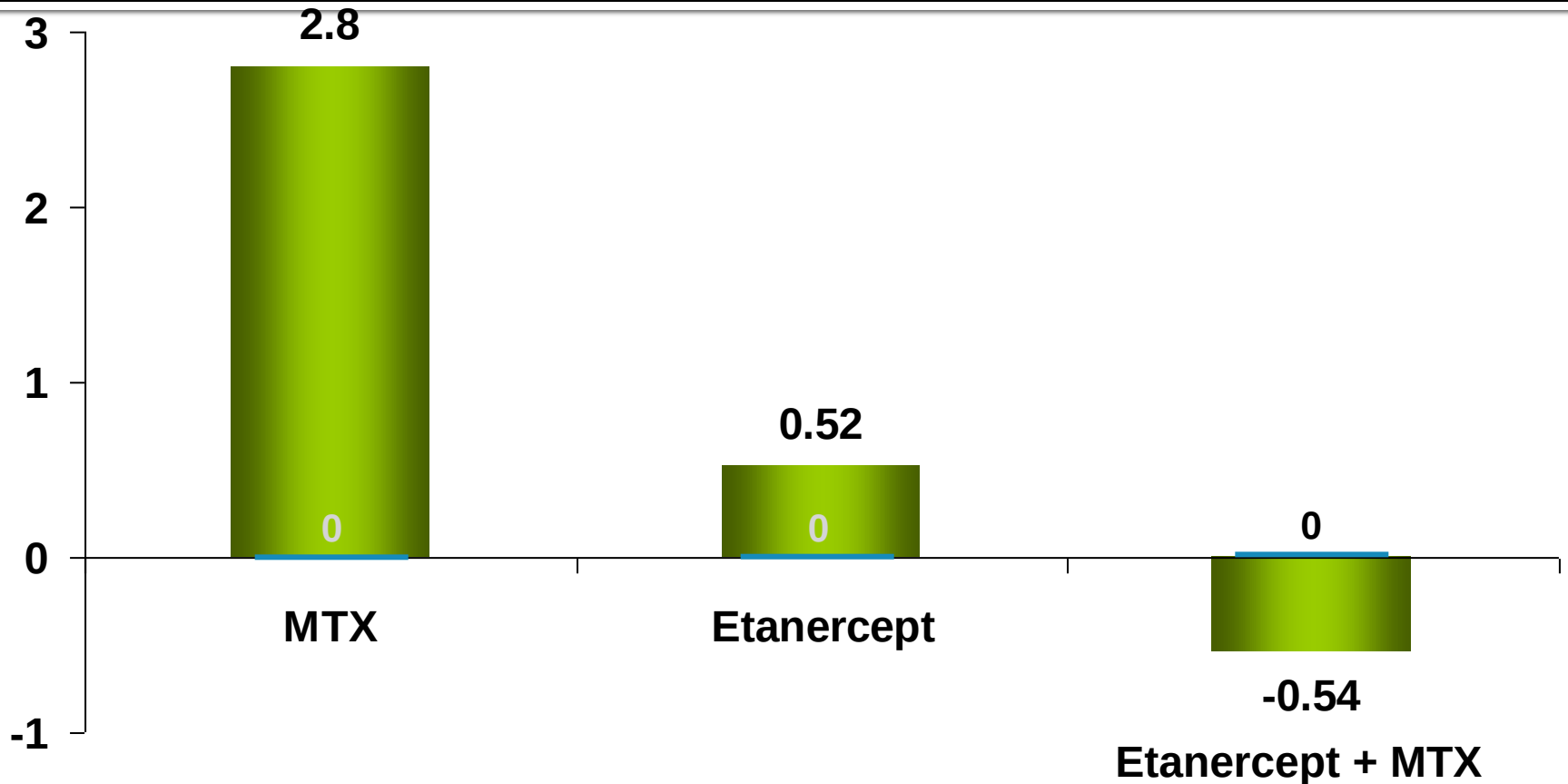


JSN: 9-point scale with 0.5
increments
13 sites/hand

0= normal
0+= questionable
1= mild (focal)
1+= mild, worse
2= moderate (loss <50%JSN)
2+= moderate, worse
3= severe (loss > 50%JSN)
3+= severe, worse
4= ankylosis or dislocation

Sharp score is a composite score of Joint Space Narrowing and Erosion in 14/13 sites. Possible scores range from 0 (perfect joints) to 400

TEMPO: Mean Change in Total Sharp Score at Week 52



Initial Management – Rheumatoid Arthritis

- In NZ, several criteria are required before access to anti-TNF agents is granted.
- Patients need to have:
 - Definite erosive rheumatoid arthritis
 - Active disease (as defined by 20 total inflamed joints, or 4 large inflamed joints)
 - Elevated inflammatory markers
 - **Despite adequate trials of adequate DMARD therapy.**
- Adequate trials of DMARD therapy include at least 3 months of therapy on so-called triple therapy (methotrexate plus sulphasalazine plus hydroxychloroquine), and also a period of at least 3 months on leflunomide or gold or cyclosporine, alone or in combination with methotrexate.

Initial Management – Rheumatoid Arthritis

- Initial therapy is always with methotrexate (assuming no contraindications).
- My personal practice in most adults is to commence 20mg on each Monday, with 10mg folic acid each Friday.
 - **(Methotrexate Monday, Folic acid Friday is an easy *aide-memoire* and ensures once-weekly prescription, avoiding the potentially fatal risk of inadvertent daily prescription and dispensing).**
 - Older or smaller patients, especially if there is renal impairment, may be started on 15mg or even 10mg weekly.
- In clear cases of RA this can be instituted by the GP.
- It takes 3 months to exert benefit, and my routine practice is to use concomitant prednisone for at least the first 3 months. Usually I prescribe 15mg/10mg/5mg daily each for 1 month then stop.
- Prednisone is used for three reasons:
 - a) to minimise the patient's symptoms,
 - b) a large body of evidence shows that prednisone is a cheap and effective means of reducing radiographic deterioration, and
 - c) in accordance with the principle of controlling disease as thoroughly as possible in the early months after diagnosis.
- The first rheumatology clinic appointment is then scheduled at the 4 month stage, when patients will have been on methotrexate for 4 months and off prednisone for a month, and so the effect of methotrexate monotherapy can be judged at the first visit and additional treatment be commenced if necessary.

Rheumatoid Arthritis: Subsequent treatment

- If the patient is not in remission, then addition of hydroxychloroquine, either alone (if disease activity is low/moderate but not in remission), or together with sulphasalazine (if disease activity is moderate/high is the next step.
- Each time a new DMARD is instituted, my personal practice is to cycle through the same 15mg/10mg/5mg/0mg each for a month before reassessing.
- Long-term low dose prednisone, substitution of leflunomide in place of the sulphasalazine, and finally anti-TNF agents are options for difficult to control disease.

Initial Management – Psoriatic Arthritis

- Methotrexate is usually the agent of first choice in cases of psoriatic arthritis and is prescribed as described above under Rheumatoid Arthritis. It has the added benefit of often being excellent for the cutaneous aspects of psoriasis.
- Depending on the patient's level of symptoms and function, prednisone may be needed in the first several weeks whilst the onset of action of methotrexate is awaited.
- Sulphasalazine and leflunomide are reasonable initial alternatives where methotrexate is not tolerated or contraindicated (although methotrexate and leflunomide share many contraindications and side effects).
- Hydroxychloroquine is often useful, but occasionally worsens the cutaneous disease.

Inflammatory Osteoarthritis

- Usually OA is readily identified by typical physical features (Heberden's and Bouchard's nodes) and by a classically mechanical history:
 - OA/mechanical/degenerative disease: best when the joint/region is resting, best at night, early morning a relatively good time, steady worsening with activity.
 - Inflammatory disease: Nocturnal and early morning pain and stiffness, improvement with activity.
- "Inflammatory OA" is considered when:
 - Inflammatory pattern to pain when physical signs point to OA
 - Erosive disease seen on X-rays
- My personal practice is when morning stiffness is a prominent feature of the presenting symptoms (lasting a minimum of 30 minutes, improving with activity) and/or there is aggressive erosive disease on X-ray, then employ a 6 month trial of methotrexate (or other DMARD). This is only continued in the presence of unequivocal improvement in the patients symptoms (quality of life)

Initial Management – Lupus /Connective Tissue Disease / ANA related arthritis

- Systemic Lupus Erythematosus is much less common than its milder, often undifferentiated counterparts. Patients with renal, pulmonary or neurological involvement or a positive dsDNA (RIA, see below) should be referred urgently to the rheumatologist.
- Note that the dsDNA is usually reported in 2 stages: an initial screening ELISA test which is highly sensitive, but has many false positives. A radioimmune (RIA) assay, sometimes called the Farr assay, is usually automatically done when the screening ELISA is positive.
- Treatment decisions aimed at full-blown lupus should only be made if the radioimmune (RIA assay, sometimes called the Farr assay) is positive.

Initial Management – Lupus /Connective Tissue Disease / ANA related arthritis

- Hydroxychloroquine (Plaquenil) is the agent first utilised for connective tissue disease-associated arthritis.
- It has efficacy against both the skin rash and arthritic manifestations of the connective tissue diseases, and may help energy levels.
- It is started at 200mg daily, this can be increased to 400mg daily.
- Photosensitive or allergic skin rashes are the main side effects.
- Patients should be counselled to be alert to photosensitivity and to employ stringent measures against UV exposure.
- Retinal toxicity is rare with modern dosing and drug choice: patients should see an optician or ophthalmologist if any visual changes occur whilst on therapy, and let them know they are taking hydroxychloroquine.

Ongoing Management - Lupus /Connective Tissue Disease / ANA related arthritis

- Often the most disabling feature of the connective tissue diseases is profound lethargy. There may also be malaise. This can be responsive to even tiny doses of prednisone. It is not uncommon for patients to report feeling well on 2mg or even 1mg of prednisone, but very unwell on any less.
- If patients are still unwell despite hydroxychloroquine, a trial of low dose (5-7.5mg daily) is often worthwhile. In responders, reduction of the dose at 1mg daily each month to identify the lowest possible effective dose is appropriate.
- More aggressive treatment with azathioprine or cyclophosphamide may be required in more aggressive cases. These should always be instituted at specialist level.

Initial Management - Spondyloarthropathies

- The spondyloarthropathies (SPA) differ greatly from the other inflammatory arthritides in that the DMARDs have repeatedly been shown to be ineffective against the axial (spinal) manifestations of the spondyloarthropathies.
 - With the exception of sulphasalazine for the peripheral joint manifestations of SPA, DMARDs have no role in management.
- Both NSAIDs and dedicated SPA-appropriate physiotherapy are of proven benefit in SPA, and most patients will respond to this.
- Disease activity is measured by a standard assessment tool named the BASDAI (Bath Ankylosing Spondylitis Activity Index). Patients who have definite SPA (including definite radiological evidence of sacroiliitis), and who have high disease activity (6/10 or greater in the BASDAI) who do not respond to adequate (3-month) trials of 2 different NSAIDs together with dedicated physiotherapy are eligible for anti-TNF therapy.

BASDAI

In the past week	Score (0-10)
Q1. How would you describe the overall level of fatigue/tiredness you have experienced?	
Q2. How would you describe the overall level of AS neck, back or hip pain you have had?	
Q3. How would you describe the overall level of pain/swelling in joints other than your neck, back or hips that you have had?	
Q4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?	
Q5. How would you describe the overall level of morning stiffness you have had from the time you wake up?	
Q6. How long does your morning stiffness last from the time you wake up? (0-2 hrs represented by 0-10 e.g. 5 = 1hr, 10 = 2hrs)	

- To score:
 - 1. Add Q1-Q4 together
 - 2. Add Q5 and Q6 together and divide by 2
 - 3. Add total 1 and 2 together and divide by 5.

Initial Management - Gout

- The initial treatment of gout is directed at the **CONSEQUENCES** of the underlying pathology: that is the extremely aggressive response of the immune system to the presence of crystals in the joint.
- **Acute gout treatment** can incorporate any or all of the following three agents:
 - NSAIDs (where not contraindicated).
 - Colchicine. 1mg initially followed 1 hour later, thereafter 0.5mg bd. **Do not give hourly until diarrhoea, gout resolution or 10 tablets have been given. This is outdated (and inhumane!)**
 - Corticosteroids (orally, intra-articularly, or intramuscularly).
 - 40-60mg daily for 3-5 days usually suffices
- **DO NOT stop allopurinol during an acute episode of gout**

Chronic Management - Gout

- Chronic gout treatment (prevention)
- Uric acid is a byproduct of purines
- Gout results from an imbalance between the production and excretion of uric acid, almost always because of subtle relative under-excretion by the kidneys (strongly genetically determined, hence the racial risk)
- Effective gout prevention therefore relies on reduction of uric acid production, increased uric acid excretion, or both.
- Avoid purine-rich foods, and alcohol (especially beer).

Medications for chronic gout management.

- Xanthine oxidase inhibitors (**BEWARE AZATHIOPRINE**)
 - Allopurinol.
 - Standard dose is 300mg daily
 - Start low and build up ESPECIALLY IN THE RENALLY IMPAIRED (risk of allopurinol hypersensitivity)
 - 600mg or 900mg can be used
 - Febuxostat
 - Licenced, not yet Pharmac funded
 - Safer in renally impaired patients
- Benzbromarone is an old and very effective agent, recently reintroduced in the NZ environment (watch LFTs)
- Colchicine 0.5mg bd often very useful prophylctically
- Probenecid 500mg up to tds as uricosuric agent
- Various intravenous uricases available in extreme patients to help dissolve tophi

